

TITLE OF THE INVENTION

PROTEIN TYROSINE PHOSPHATASE-1B (PTP-1B) DEFICIENT MICE AND
ASSAYS FOR PTP-1B MODULATORS

5 ABSTRACT OF THE DISCLOSURE

The present invention provides mice that have had their PTP-1B genes disrupted by targeted homologous recombination. The mice have no detectable PTP-1B protein, yet appear to be physiologically normal. However, in the fed state on a normal diet, the mice have half the level of circulating insulin as their wild-type littermates. In glucose and insulin tolerance tests, the mice show an increased insulin sensitivity. When fed a high fat, high carbohydrate diet, the mice show a resistance to weight gain as compared to their wild-type littermates.

Methods of making the mice and cell lines derived from the mice are also provided.

15 The present invention also provides methods of identifying inhibitors of the enzymatic activity of PTP-1B as well as inhibitors identified by such methods.